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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,463	01/16/2004	Hiraku Itadani	14871-083002 / B1-103PCT-	7593

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EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 08/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/759,463	ITADANI ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *36-38,42-44,46-48 and 50* is/are allowed.

6)☒ Claim(s) *39,41,45,49,51 and 53-59* is/are rejected.

7)☒ Claim(s) *40 52* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/891,053.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/16/04, 1/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1) Claims 36 to 59 are pending in the instant application. Claims 1 to 35 have been canceled and claims 36 to 59 have been added as requested by Applicant in the correspondence filed 08 November of 2004.

2) Claims 36 to 38, 42 to 44, 46 to 48 and 50 are allowable as written.

3) Claims 40 and 52 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4) Claims 39, 41, 45, 49, 51 and 53 to 59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the production and use of an isolated nucleic acid encoding protein comprising the amino acid sequence presented in SEQ ID NO:20 and 25 of the instant specification or specific portions thereof, it does not reasonably provide an adequate written description of any other polypeptide which functions as a histamine receptor, or the guidance needed to make it. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 53, for example, encompasses an isolated nucleic acid comprising a nucleotide sequence that is at least 70% "homologous" to SEQ ID N0:21 or SEQ ID NO: N0:26 of the instant application, "wherein the nucleic acid encodes a polypeptide that has an activity of a G protein-coupled receptor protein". Because a single amino acid

residue in a protein is encoded by three consecutive nucleotides constituting a codon, and the modification of a single nucleotide in a codon can be sufficient to change the amino acid residue encoded thereby, claim 53 encompasses a nucleic acid encoding receptor protein whose amino acid sequence can deviate from SEQ ID NO:20 or 25 **by up to 90%** of the amino acid residues in that sequence. The claims are not enabled because an artisan does not have a reasonable expectation that a protein whose amino acid sequence has been altered by up to 90% is going to retain functionality or structural integrity.

The instant specification discloses that a polypeptide comprising the amino acid sequence presented in either SEQ ID NO:20 or 25 of the instant specification corresponds to a naturally occurring protein which is a histamine-activated member of the family of proteins known as G protein-coupled receptors. It further discloses that a protein comprising one of the two amino acid sequences presented in SEQ ID NO:20 and 25 can be used to identify ligands which may be potentially pharmacologically relevant. The information derived therefrom, however, is only relevant in so far as it is applicable to a native protein.

Whereas the instant claims potentially encompass tens of thousands, if not millions, of naturally and non-naturally occurring embodiments, the instant specification only describes two working examples of isolated nucleic acids and those two examples encode two naturally occurring orthologues of a common protein. The instant specification does not provide even one working example of an isolated nucleic acid encoding a functional receptor protein of the instant invention whose amino acid

sequence deviates from nature by as little as a single amino acid sequence, much less the 405 residues permitted by claim 53. Further, the instant specification does not identify those amino acid residues in the amino acid sequence of SEQ ID NO:20 or 25 which are essential for the biological activity and structural integrity of a histamine receptor comprising that sequence and those residues which are either expendable or substitutable, nor does it identify a structurally related protein in the prior art for which this information is known and could be applied to a protein encoded by the claimed nucleic acid by analogy. In the absence of such structure-function information a practitioner would have to resort to a substantial amount of undue experimentation in the form of insertional, deletional and substitutional mutation analysis of over 450 amino acid residues before they could even begin to rationally design an isolated nucleic acid encoding a functional histamine receptor polypeptide having other than one of the two natural amino acid sequences presented in the specification.

As disclosed in the instant specification, a protein encoded by an isolated nucleic acid of the instant invention is a member of the G protein-coupled receptor family. By definition, all of the proteins belonging to this family share a complex serpentine structure comprising four extracellular domains, seven transmembrane domains and four cytoplasmic domain. The ligand binding activity of the subfamily of receptors to which the instant invention belongs, which includes adrenergic and dopamine receptors, is generally attributed to interactions between a ligand, various amino acid side chains extending from several different extracellular and transmembrane domains and the

hydrophobic pocket formed by those transmembrane domains. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Given the complex structure of a protein encoded by a nucleic acid of the instant invention, and the lack of working examples and guidance in the predictable alteration of such proteins, and artisan could not reasonably produce an isolated nucleic acid encoding a receptor protein of the instant invention whose amino acid sequence deviates from either of those two sequences recited in the claims by any more than three amino acid residues and reasonably "predict by resort to known scientific law" whether that protein will function as a histamine receptor and, more important, whether that protein will perform in a manner that is predictive of a native protein. The only specific and substantial disclosed utility for the protein encoded by the claimed nucleic acid is in the identification of pharmacologically useful compounds. If a protein which meets all of the current limitations of the instant claims does not function in a

manner that is predictive of a native protein in its natural environment then the instant specification fails to disclose how to use that protein.

Further, these claims encompass subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims encompass, for example, an "isolated nucleic acid comprising a nucleotide sequence that is at least 70% homologous to SEQ ID NO:21 or SEQ ID NO:26" wherein said nucleic acid "encodes a polypeptide that has an activity of a G protein-coupled receptor". It is a routine matter for an artisan to identify those members of the genus of nucleic acids which meet the first two limitations of being an "isolated nucleic acid" and "is at least 70% homologous to SEQ ID NO:21 or SEQ ID NO:26". However, one of ordinary skill would not reasonably expect that the majority of nucleic acids belonging to that genus would also meet the limitation "encodes a polypeptide that has an activity of a G protein-coupled receptor". One would not reasonably expect the functional limitation of the instant claims to inherently flow from the structural limitations recited therein. Further, the instant specification does not identify that physical property of combination of physical properties that can be used to distinguish those nucleic acids which meet the functional limitation of the claims from those that don't. The inclusion of a functional limitation in the claims in the absence of a recitation of those material features which provide that function constitutes nothing more than a wish to know the identity of any nucleic acid which meets all of the limitations of the claims. In the decision *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), the court held that:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

Whereas the instant specification provides a detailed description of two naturally occurring nucleic acids which encode two naturally occurring proteins that meet all of the limitations of the claims, the instant specification does not provide a written description of the genus of nucleic acids encompassed thereby or even a representative number of the potentially tens of thousands, or millions, of non-naturally occurring embodiments currently claimed.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

6) Claims 39, 41, 45, 49, 51 and 53 to 59 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by the Goodearl et al. patent (5,882,893, cited by Applicant). The Goodearl et al. patent described an isolated polypeptide comprising the

amino acid sequence presented in SEQ ID NO:2 therein, which is identical to the first 445 amino acid residues of SEQ ID NO:20 of the instant application. The isolated nucleic acid presented in SEQ ID NO:1 of Goodearl et al. clearly meets all of the limitations of the instant claims because the coding sequence presented therein is greater than 95% identical to the coding sequence presented in SEQ ID NO:21 of the instant application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN ULM
PRIMARY EXAMINER
GROUP 1600